

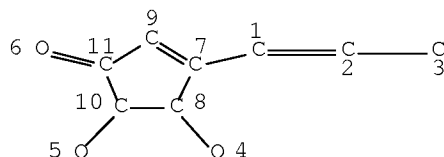
Inventor search history

=> d his L83

(FILE 'HCAPLUS' ENTERED AT 16:12:43 ON 28 MAR 2008)

L83 7 S L81 OR L82

=> d que L83

L2 1 SEA FILE=REGISTRY ABB=ON PLU=ON 582-46-7/RN
L4 STR

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

L6 9 SEA FILE=REGISTRY FAM FUL L4
 L9 62 SEA FILE=HCAPLUS ABB=ON PLU=ON L2
 L10 69 SEA FILE=HCAPLUS ABB=ON PLU=ON L6
 L68 160 SEA FILE=HCAPLUS ABB=ON PLU=ON ("YOO ICH DONG"/AU OR "YOO
 ICK D"/AU OR "YOO ICK DOG"/AU OR "YOO ICK DONG"/AU OR "YOO ICK
 JONG"/AU OR "YOO ICKDONG"/AU)
 L69 79 SEA FILE=HCAPLUS ABB=ON PLU=ON "KIM WON GON"/AU
 L70 46 SEA FILE=HCAPLUS ABB=ON PLU=ON "RYOO IN JA"/AU
 L71 52 SEA FILE=HCAPLUS ABB=ON PLU=ON ("KIM JONG PYONG"/AU OR "KIM
 JONG PYUNG"/AU)
 L72 48 SEA FILE=HCAPLUS ABB=ON PLU=ON "LEE SANGKU"/AU
 L73 30 SEA FILE=HCAPLUS ABB=ON PLU=ON "LEE SANG KU"/AU
 L74 27 SEA FILE=HCAPLUS ABB=ON PLU=ON ("PARK SEO HYEONG"/AU OR
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 L75 4 SEA FILE=HCAPLUS ABB=ON PLU=ON ("PARK SEOHYOUNG"/AU OR "PARK
 SEOHYUNG"/AU)
 L76 210 SEA FILE=HCAPLUS ABB=ON PLU=ON ("KIM DONG SEOCK"/AU OR "KIM
 DONG SEOG"/AU OR "KIM DONG SEOK"/AU)
 L77 55 SEA FILE=HCAPLUS ABB=ON PLU=ON "PARK KYOUNG CHAN"/AU
 L78 1 SEA FILE=HCAPLUS ABB=ON PLU=ON "YOO ICKDONG"/AU
 L80 508 SEA FILE=HCAPLUS ABB=ON PLU=ON (L68 OR L69 OR L70 OR L71 OR
 L72 OR L73 OR L74 OR L75 OR L76 OR L77 OR L78)
 L81 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L80 AND TERREIN
 L82 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L80 AND (L9 OR L10)
 L83 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L81 OR L82

=> d his L93

(FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 17:03:12 ON 28 MAR 2008)

L93 9 S L81

=> d que L93

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L68      160 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("YOO ICH DONG"/AU OR "YOO
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L70      46 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "RYOO IN JA"/AU
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          JONG PYUNG"/AU)
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L74      27 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("PARK SEO HYEONG"/AU OR
          "PARK SEO HYOUNG"/AU)
L75      4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("PARK SEOHYOUNG"/AU OR "PARK
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L76      210 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("KIM DONG SEOCK"/AU OR "KIM
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L77      55 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "PARK KYOUNG CHAN"/AU
L78      1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "YOO ICKDONG"/AU
L80      508 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L68 OR L69 OR L70 OR L71 OR
          L72 OR L73 OR L74 OR L75 OR L76 OR L77 OR L78)
L81      7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L80 AND TERREIN
L93      9 SEA L81

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=> dup rem L83 L93

FILE 'HCAPLUS' ENTERED AT 17:29:23 ON 28 MAR 2008
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 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'MEDLINE' ENTERED AT 17:29:23 ON 28 MAR 2008

FILE 'BIOSIS' ENTERED AT 17:29:23 ON 28 MAR 2008

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PROCESSING COMPLETED FOR L83

PROCESSING COMPLETED FOR L93

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L134      10 DUP REM L83 L93 (6 DUPLICATES REMOVED)
          ANSWERS '1-7' FROM FILE HCAPLUS
          ANSWERS '8-10' FROM FILE MEDLINE

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Inventor search history

=> d L134 1-10 ibib ab

L134 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2008:256581 HCAPLUS Full-text
 TITLE: The hypopigmentary action of KI-063 (a new tyrosinase inhibitor) combined with terrein
 AUTHOR(S): Kim, Dong-Seok; Lee, Sangku; Lee, Hyun-Kyung; Park, Seo-Hyoung; Ryoo, In-Ja; Yoo, Ick-Dong; Kwon, Sun-Bang; Baek, Kwang Jin; Na, Jung-Im; Park, Kyoung-Chan
 CORPORATE SOURCE: Department of Biochemistry, College of Medicine, Chung-Ang University, Seoul, 156-756, S. Korea
 SOURCE: Journal of Pharmacy and Pharmacology (2008), 60(3), 343-348
 CODEN: JPPMAB; ISSN: 0022-3573
 PUBLISHER: Pharmaceutical Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Resorcinol derivs. are known to inhibit melanin synthesis. In this study, resorcinol derivs. were synthesized and screened for their activity on melanogenesis. KI-063 (a tyrosinase inhibitor) was examined for its effects on melanogenesis using a spontaneously immortalized mouse melanocyte cell line (Mel-Ab). In a cell-free system, KI-063 directly inhibited tyrosinase, the rate-limiting melanogenic enzyme. Moreover, in a cell system, it inhibited melanin synthesis in a concentration-dependent manner. In addition, KI-063 inhibited the activity of cellular tyrosinase. Thus, this study examined the effects of a combination of KI-063 with terrein, an agent that down-regulates microphthalmia-associated transcription factor. The data suggest that KI-063 has an additive effect in combination with terrein. Thus, the suppression of tyrosinase activity by KI-063 and the inhibition of tyrosinase production by terrein appear to be an optimal combination for skin whitening.

L134 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2005:1082506 HCAPLUS Full-text
 DOCUMENT NUMBER: 144:250065
 TITLE: Terrein, a melanin biosynthesis inhibitor, from Penicillium sp. 20135
 AUTHOR(S): Kim, Won-Gon; Ryoo, In-Ja; Park, Seo-Hyoung; Kim, Dong-Seok; Lee, Sangku; Park, Kyoung-Chan; Yoo, Ick-Dong
 CORPORATE SOURCE: Korea Research Institute of Bioscience and Biotechnology, Daejeon, 305-600, S. Korea
 SOURCE: Journal of Microbiology and Biotechnology (2005), 15(4), 891-894
 CODEN: JOMBES; ISSN: 1017-7825
 PUBLISHER: Korean Society for Microbiology and Biotechnology
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB A melanin biosynthesis inhibitor, named terrein (I), 4,5-dihydroxy-3-propenyl-2-cyclopenten-1-one was isolated from Penicillium sp. I had a strong inhibitory activity on melanin formation in B16 melanoma and melanocyte Mel-Ab cells.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2004:1124990 HCAPLUS Full-text

DOCUMENT NUMBER: 142:214971

TITLE: Synthesis and melanin biosynthesis inhibitory activity of (\pm)-terrein produced by *Penicillium* sp. 20135

AUTHOR(S): Lee, Sangku; Kim, Won-Gon; Kim, Eungsoo; Ryoo, In-Ja; Lee, Hyeong Kyu; Kim, Jae Nyoung; Jung, Sang-Hun; Yoo, Ick-Dong

CORPORATE SOURCE: Korea Research Institute of Bioscience and Biotechnology, Taejon, 305-333, S. Korea

SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(2), 471-473

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 142:214971

AB Terrein (I) was isolated from *Penicillium* sp. 20135, prepared by a practical synthetic way, and evaluated for its melanin biosynthesis inhibitory activity.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1369953 HCAPLUS Full-text

DOCUMENT NUMBER: 148:17709

TITLE: Skin keratinocyte proliferation inhibitor containing terrein

INVENTOR(S): Yoo, Ik Dong; Yoo, In Ja; Kim, Won Gon; Kim, Jong Pyeong; Park, Seo Hyeong; Kim, Dong Seok; Kwon, Seon Bang

PATENT ASSIGNEE(S): Korea Research Institute of Bioscience and Biotechnology, S. Korea; Welskin Co., Ltd.

SOURCE: Repub. Korean Kongkae Taeho Kongbo, 10pp.

CODEN: KRXXA7

DOCUMENT TYPE: Patent

LANGUAGE: Korean

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
KR 2007100046	A	20071010	KR 2006-31595	20060406
KR 771523	B1	20071030		

PRIORITY APPLN. INFO.: KR 2006-31595 20060406

AB In the invention, terrein is isolated from *Penicillium* sp. strain. Terrein has melanin synthesis inhibition effect and keratinocyte proliferation inhibition effect. The title inhibitor can be used in therapeutic agents or therapeutic aid of psoriasis, allergic dermatitis, flat lichen, keratosis, and basal cell carcinoma.

L134 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:271409 HCAPLUS Full-text

DOCUMENT NUMBER: 147:228448

TITLE: Terrein, a fungal metabolite, inhibits the epidermal proliferation of skin equivalents

AUTHOR(S): Kim, Dong-Seok; Cho, Hyun-Joo; Lee, Hyun-Kyung; Lee, Woong-Hee; Park, Eun-Sang; Youn,

10/596,211

CORPORATE SOURCE: Sang-Woong; Park, Kyoung-Chan
 Department of Dermatology, Seoul National University
 College of Medicine, Seoul, 110-744, S. Korea
 SOURCE: Journal of Dermatological Science (2007), 46(1), 65-68
 CODEN: JDSCEI; ISSN: 0923-1811
 PUBLISHER: Elsevier Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB In order to study the effects of terrein on the epidermal proliferation, skin equivalent (SEs) were treated with terrein during air-liquid exposure for 7 or 10 days, resp. Media containing terrein were changed every other day. H&E results after 13 days of culture showed that control SEs constructs had a regular stratification of thick epidermis, whereas terrein-treated SEs had a relatively thin epidermis, and a poorer fabricated horny layer. Results demonstrate that terrein has a strong antiproliferative effect on human SEs, and suggest that terrein could be developed to treat hyperproliferative skin diseases such as psoriasis vulgaris.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:540480 HCAPLUS Full-text

DOCUMENT NUMBER: 143:83184

TITLE: Terrein compound having melanin biosynthesis inhibitors and its preparation

INVENTOR(S): Yoo, Ick-Dong; Kim, Won-Gon;
 Ryoo, In-Ja; Kim, Jong-Pyung;
 Lee, Sangku; Park, Seo-Hyoung;
 Kim, Dong-Seok; Park, Kyoung-Chan

PATENT ASSIGNEE(S): Korea Research Institute of Bioscience and
 Biotechnology, S. Korea; Welskin Co., Ltd.

SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005055995	A1	20050623	WO 2004-KR2677	20041019
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1691796	A1	20060823	EP 2004-793535	20041019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1925848	A	20070307	CN 2004-80036912	20041019
JP 2007513941	T	20070531	JP 2006-543731	20041019
US 2007128136	A1	20070607	US 2006-596211	20060602
PRIORITY APPLN. INFO.:			KR 2003-90611	A 20031212
			WO 2004-KR2677	W 20041019

AB The present invention relates to a melanin biosynthesis inhibitor containing ~~terrein~~ compound as an effective ingredient. The ~~terrein~~ compound can be easily separated from Penicillium sp. KCTC 26245, a fungal strain inhabiting domestic soil. It does not directly inhibit tyrosinase but inhibits the expression of MITF (microphthalmia-associated transcription factor) by activating ERK (extracellular signal-regulated kinase) in melanin chromatocytes to give whitening effect. So, the melanin biosynthesis inhibiting effect of the compound is much greater than that of any other conventional inhibitors, and further the effect can be raised when the compound is used together with other inhibitors, owing to their different mechanisms. Thus, the compound of the present invention can be effectively used as a skin trouble treating agent, a skin whitening agent and a browning inhibitor.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L134 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1014077 HCAPLUS Full-text

DOCUMENT NUMBER: 146:206142

TITLE: Preparation of ~~terrein~~ compound via formation of 5-(1,1-Dimethylethoxy)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(E)-1-propenyl]-2-cyclopenten-1-one and reaction sequence involving Grignard reaction, oxidative rearrangement and isomerization

INVENTOR(S): Yoo, Ik Dong; Lee, Sang Ku; Yoo, In Ja; Kim, Won Gon; Kim, Jong Pyung

PATENT ASSIGNEE(S): Korea Research Institute of Bioscience and Biotechnology, S. Korea

SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7

DOCUMENT TYPE: Patent

LANGUAGE: Korean

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
KR 2005116055	A	20051209	KR 2004-40956	20040604
PRIORITY APPLN. INFO.:			KR 2004-40956	20040604

AB A method for preparing a ~~terrein~~ compound [i.e., 4,5-dihydroxy-3-(1E)- 1-propenyl-2-cyclopenten-1-one from Penicillium fungus] under the mild and economical conditions with an excellent yield is claimed. The method comprises the reaction of furfuryl alc. with a bromination agent and acetic anhydride to provide 6-acetoxy-2,6-dihydro-3H-pyran-3-one. Furthermore the acetoxy group of the 6-acetoxy-2,6-dihydro-3H-pyran-3-one is converted into a tert-butoxy group to provide 6-tert-butoxy-2,6-dihydro- 3H-pyran-3-one. Then, 4-tert-butoxy-5-hydroxy-cyclopent-2-en-1-one is prepared by ring contraction. A tert-butyldimethylsilyl protecting group is introduced to the hydroxy group of the 4-tert-butoxy-5-hydroxy-cyclopent-2- en-1-one. Treatment of the 4-tert-butoxy-5-tert-butyldimethylsilyloxy- cyclopent-2-en-1-one with an allyl magnesium bromide provides 1-allyl-4-t-butoxy-5-t-butyldimethylsilyloxy-cyclopent-2-en-1-one. Oxidative rearrangement provides 5-tert-butoxy-4-tert-butyldimethylsilyloxy-3-allyl-cyclopent-2-en-1-one. Isomerization provides 5-tert-butoxy-4-tert-butyldimethylsilyloxy-3-(E)-propen-1-yl- cyclopent-2-en-1-one. The tert-Bu protecting group is removed by using a Lewis acid and the tert-butyldimethylsilyl group is removed by acid cleavage.

ACCESSION NUMBER: 2007229842 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 17197159
 TITLE: Terrein, a fungal metabolite, inhibits the epidermal proliferation of skin equivalents.
 AUTHOR: Kim Dong-Seok; Cho Hyun-Joo; Lee Hyun-Kyung; Lee Woong-Hee; Park Eun-Sang; Youn Sang-Woong; Park Kyoung-Chan
 SOURCE: Journal of dermatological science, (2007 Apr) Vol. 46, No. 1, pp. 65-8. Electronic Publication: 2007-01-02. Journal code: 9011485. ISSN: 0923-1811.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Letter
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200705
 ENTRY DATE: Entered STN: 19 Apr 2007
 Last Updated on STN: 17 May 2007
 Entered Medline: 16 May 2007

L134 ANSWER 9 OF 10 MEDLINE on STN
 ACCESSION NUMBER: 2008201011 IN-PROCESS Full-text
 DOCUMENT NUMBER: PubMed ID: 18358890
 TITLE: Terrein reduces pulpal inflammation in human dental pulp cells.
 AUTHOR: Lee Jung-Chang; Yu Mi-Kyung; Lee Rin; Lee Young-Hee; Jeon Jae-Gyu; Lee Min-Ho; Jhee Eun-Chung; Yoo Ick-Dong; Yi Ho-Keun
 CORPORATE SOURCE: Department of Oral Biochemistry, School of Dentistry, Chonbuk National University, Jeonbuk, Korea.
 SOURCE: Journal of endodontics, (2008 Apr) Vol. 34, No. 4, pp. 433-7. Journal code: 7511484. ISSN: 0099-2399.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Dental Journals
 ENTRY DATE: Entered STN: 25 Mar 2008
 Last Updated on STN: 25 Mar 2008

AB Terrein is a bioactive fungal metabolite whose anti-inflammatory properties are virtually unknown. The purpose of this study was to determine the effects of terrein on lipopolysaccharide (LPS)-induced expression of intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) in human dental pulp cells and to determine the mechanism of the observed effects. The LPS-induced expression of ICAM-1 and VCAM-1 was inhibited by terrein in both a time- and dose-dependent manner. LPS-stimulated translocation of nuclear factor kappa B (NF-kappaB) into the nucleus, which was blocked by inhibitors of amino kinase terminal (AKT, LY294002), extracellular signal regulated kinase 1/2 (ERK 12, PD98059), p38 (SB203580), and c-jun NH2-terminal kinase (JNK, SP600125) or terrein. In addition, these inhibitors and terrein also reduced the level of ICAM-1 and VCAM-1 expression in LPS-induced inflammation of pulp cells. Terrein suppressed NF-kappaB activation by blocking the activation of Akt. These results strongly suggest the potential role of terrein as an anti-inflammatory modulator in pulpal inflammation.

L134 ANSWER 10 OF 10 MEDLINE on STN
 ACCESSION NUMBER: 2008155552 IN-PROCESS Full-text
 DOCUMENT NUMBER: PubMed ID: 17979972

TITLE: Terrein inhibits keratinocyte proliferation via
ERK inactivation and G2/M cell cycle arrest.

AUTHOR: Kim Dong-Seok; Lee Hyun-Kyung; Park
Seo-Hyoung; Lee Sangku; Ryoo In-Ja
; Kim Won-Gon; Yoo Ick-Dong; Na
Jung-Im; Kwon Sun-Bang; Park Kyoung-Chan

CORPORATE SOURCE: Department of Biochemistry, College of Medicine, Chung-Ang
University, Republic of Korea.

SOURCE: Experimental dermatology, (2008 Apr) Vol. 17, No. 4, pp.
312-7. Electronic Publication: 2007-11-02.
Journal code: 9301549. E-ISSN: 1600-0625.

PUB. COUNTRY: Denmark

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 5 Mar 2008
Last Updated on STN: 5 Mar 2008

AB Terrein, a fungal metabolite, has been recently shown to have a strong antiproliferative effect on skin equivalents. In the present study, we further investigated the effects of terrein on the possible signalling pathways involved in the growth inhibition of human epidermal keratinocytes by examining the regulations of extracellular signal-regulated protein kinase (ERK) and of the Akt pathway by terrein. It was observed that ERK was inactivated by terrein and that keratinocyte proliferation was inhibited, whereas Akt was unaffected. The inhibition of the ERK pathway by U0126 (a specific ERK inhibitor) also had a dose-dependent antiproliferative effect on human keratinocytes. These results indicate that ERK inhibition is involved in keratinocyte growth inhibition by terrein. Moreover, flow cytometric analysis showed that terrein inhibits DNA synthesis, as evidenced by a reduction in the S phase and an increase in the G2/M phase of the cell cycle. Thus, we next examined changes in the expressions of G2/M cell cycle-related proteins. Terrein was found to downregulate cyclin B1 and Cdc2 without Cdc2 phosphorylation, but upregulated p27(KIP1) (p27), a known inhibitor of cyclin-dependent kinase. These results suggest that terrein reduces human keratinocyte proliferation by inhibiting ERK and by decreasing the expressions of cyclin B1 and Cdc2 complex.

The chemical structure shows a five-membered ring with alternating double bonds and five chlorine atoms. The atoms are numbered as follows: 1 is the carbon atom on the right double bond; 2 is the chlorine atom bonded to it; 3 is the carbon atom on the right single bond; 4 is the chlorine atom bonded to it; 5 is the carbon atom at the bottom; 6 is the chlorine atom bonded to it; 7 is the carbon atom at the top; 8 is the chlorine atom bonded to it; 9 is the carbon atom on the left double bond; 10 is the chlorine atom bonded to it; 11 is the carbon atom on the left single bond.

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L6          9 SEA FILE=REGISTRY FAM FUL L4
L7          1 SEA FILE=REGISTRY ABB=ON  PLU=ON  142243-02-5/RN
L9          62 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L2
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L11        14053 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L7
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L13         N? OR CYCLO(W)PENTEN?)
L13         QUE  ABB=ON  PLU=ON  ((SKIN? OR DERM? OR EPIDERM? OR COMP
L14         LECTION? OR COMPLEXION? OR CUTICL?) (3A) (TROUBLE OR CONDIT
L14         ION OR BLOTCH? OR SPOT? OR LIVER? OR AGING? OR AGE OR WHI
L14         TEN? OR BROWN? OR MELANIN))
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L15         INHIBIT?))
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L18         1 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L9 AND L11
L19         1 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L10 AND L11
L20         0 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L9 AND L12
L21         1 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L9 AND L13
L22         4 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L9 AND L14
L23         3 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L9 AND L15
L24         7 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L10 NOT L9
L25         0 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L24 AND L12
L26         0 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L24 AND L13
L27         1 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L24 AND L14
L28         0 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L24 AND L15
L29         QUE  ABB=ON  PLU=ON  ((LIVER? OR AGE OR AGING OR BROWN? O
L29         R OLD?) (3A) (SPOT? OR BLOTCH? OR MARK? OR SIGN? OR SKIN? O
L29         R HAND?))
L30         0 SEA FILE=HCAPLUS  ABB=ON  PLU=ON  L9 AND L29

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10/596,211

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L31      0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND L29
L32      0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND L12
L33      2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND L13
L34      6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND L14
L35      3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND L15
L36     1712 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PENICILLIUM(5A) (STRAIN OR
        "KCTC" OR "KCTC(W)262245")
L37      3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L9
L38      3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L10
L39      3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L17
L40      0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L12
L41      1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L13
L42      3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L14
L43     12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L18 OR L19 OR L20 OR L21 OR
        L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28)
L44      7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L30 OR L31 OR L32 OR L33 OR
        L34 OR L35)
L45      4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L37 OR L38 OR L39 OR L40 OR
        L41 OR L42)
L46     14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L43 OR L44 OR L45)
L47      QUE ABB=ON  PLU=ON  AY<2004 OR PY<2004 OR PRY<2004 OR MY
        <2004 OR REVIEW/DT
L48      9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L46 AND L47
L49     69 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR L10
L50     58 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 AND L47
L51     56 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L50 AND TERREIN
L52      0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND "MELANIN BIOSYNTHESIS
        INHIBIT?"
L53      1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND "MELANIN BIOSYNTHESIS"
L54      0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND "MELANIN(3N) INHIBIT?"
L55      1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND MELANIN
L56      9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND BIOSYNTHES?
L57      7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND INHIBIT?
L58     15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L52 OR L53 OR L54 OR L55 OR
        L56 OR L57)
L59      1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L58 AND (MELANIN OR SKIN OR
        DERM?)
L60      0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND L12
L61      1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND L13
L62      1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND L14
L63      2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND L15
L64      2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L59 OR L60 OR L61 OR L62 OR
        L63)
L65      9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L64 OR L48
L66      1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L51 AND BIOSYNTH? AND MELANIN
        AND (INHIBIT? OR BLOCK?)
L67      9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 OR L66

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=> d his L92

(FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 17:03:12 ON 28 MAR 2008)

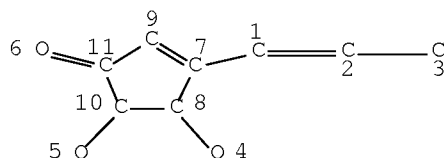
L92 9 S L88-L91

=> d que L92

```

L2      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  582-46-7/RN
L4      STR

```



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

```

L6          9 SEA FILE=REGISTRY FAM FUL L4
L9          62 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L10         69 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6
L12         QUE ABB=ON  PLU=ON  (CYCLO(W)PENTADIEN? OR CYCLO(W)PENTA
N? OR CYCLO(W)PENTEN?)
L13         QUE ABB=ON  PLU=ON  ((SKIN? OR DERM? OR EPIDERM? OR COMP
LECTION? OR COMPLEXION? OR CUTICL?) (3A) (TROUBLE OR CONDIT
ION OR BLOTCH? OR SPOT? OR LIVER? OR AGING? OR AGE OR WHI
TEN? OR BROWN? OR MELANIN))
L14         QUE ABB=ON  PLU=ON  ((BROWN? OR MELANIN) (3A) (SYNTHESE? OR
INHIBIT?))
L15         QUE ABB=ON  PLU=ON  PENICILLIUM(5A) (STRAIN OR "KCTC" OR
"KCTC(W)262245")
L84         44 SEA L9
L85         45 SEA L10
L86         45 SEA L84 OR L85
L87         45 SEA L86 AND TERREIN
L88         2 SEA L87 AND L12
L89         1 SEA L87 AND L13
L90         7 SEA L87 AND L14
L91         1 SEA L87 AND L15
L92         9 SEA (L88 OR L89 OR L90 OR L91)

```

=> d his L104

(FILE 'MEDLINE' ENTERED AT 17:08:02 ON 28 MAR 2008)

L104 2 S L100 AND L98

=> d que L104

```

L98         5353 SEA FILE=MEDLINE ABB=ON  PLU=ON  PENICILLIUM/CT
L100        39 SEA FILE=MEDLINE ABB=ON  PLU=ON  TERREIN?
L104        2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L100 AND L98

```

=> d his L119

(FILE 'BIOSIS' ENTERED AT 17:13:14 ON 28 MAR 2008)

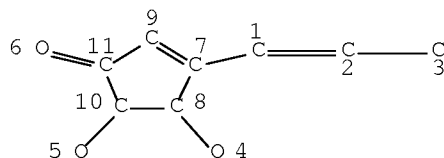
L119 4 S L117 OR L118

=> d que L119

L2 1 SEA FILE=REGISTRY ABB=ON PLU=ON 582-46-7/RN

L4

STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

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L6          9 SEA FILE=REGISTRY FAM FUL L4
L106        19 SEA FILE=BIOSIS ABB=ON  PLU=ON  L2
L107        20 SEA FILE=BIOSIS ABB=ON  PLU=ON  L6
L108        5886 SEA FILE=BIOSIS ABB=ON  PLU=ON  COSMETICS/CT
L109        5151 SEA FILE=BIOSIS ABB=ON  PLU=ON  ("MELANIELLA "/CT OR "MELANIFER
OUS ZONA"/CT OR MELANIN/CT OR "MELANIN "/CT OR "MELANIN A"/CT
OR "MELANIN AFFINITY"/CT OR "MELANIN ALLERGY"/CT OR "MELANIN
ANALOGUE"/CT OR "MELANIN ASSOCIATED ANTIGEN"/CT OR "MELANIN
BINDING PROPERTIES"/CT OR "MELANIN BIOSYNTHESIS"/CT OR
"MELANIN BIOSYNTHESIS DEHYDRATASE INHIBITOR"/CT OR "MELANIN
BIOSYNTHESIS GENES"/CT OR "MELANIN BIOSYNTHESIS INHIBITOR"/CT
OR "MELANIN BIOSYNTHESIS INHIBITOR-CONTAINING COMPOSITION"/CT
OR "MELANIN BIOSYNTHETIC ENZYMES"/CT OR "MELANIN BIOSYNTHETIC
PATHWAY INTERMEDIATE"/CT OR "MELANIN BLEACH"/CT OR "MELANIN
BLEACHING"/CT OR "MELANIN CELLS"/CT OR "MELANIN COLORATION"/CT
OR "MELANIN COLUMNS"/CT OR "MELANIN COMPLEX"/CT OR "MELANIN
COMPLEXES"/CT OR "MELANIN CONCENTRATING HORMONE"/CT OR
"MELANIN CONCENTRATING HORMONE 1"/CT OR "MELANIN CONCENTRATING
HORMONE 1 RECEPTOR"/CT OR "MELANIN CONCENTRATING HORMONE 2
RECEPTOR"/CT OR "MELANIN CONCENTRATING HORMONE ANTAGONIST"/CT
OR "MELANIN CONCENTRATING HORMONE ANTAGONIST 1"/CT OR "MELANIN
CONCENTRATING HORMONE ANTAGONISTS"/CT OR "MELANIN CONCENTRATING
HORMONE MESSENGER RNA"/CT OR "MELANIN CONCENTRATING HORMONE
MRNA"/CT OR "MELANIN CONCENTRATING HORMONE NEURONAL POPULATION"
/CT OR "MELANIN CONCENTRATING HORMONE PRECURSOR MRNA"/CT OR
"MELANIN CONCENTRATING HORMONE R1 ANTAGONIST"/CT OR "MELANIN
CONCENTRATING HORMONE RECEPTOR"/CT OR "MELANIN CONCENTRATING
HORMONE RECEPTOR 1"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR 1 ANTAGONIST"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR 1 ANTAGONISTS"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR 2"/CT OR "MELANIN CONCENTRATING HORMONE RECEPTOR
AGONISTS"/CT OR "MELANIN CONCENTRATING HORMONE RECEPTOR
ANTAGONIST"/CT OR "MELANIN CONCENTRATING HORMONE RECEPTOR
CHIMERIC PROTEIN"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR FUSION PROTEIN"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR LIGANDS"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR MESSENGER RNA"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR MRNA"/CT OR "MEL
L110        3 SEA FILE=BIOSIS ABB=ON  PLU=ON  PENICILLIUM/CT
L111        20 SEA FILE=BIOSIS ABB=ON  PLU=ON  L106 OR L107
L112        0 SEA FILE=BIOSIS ABB=ON  PLU=ON  L111 AND (L108 OR COSMETIC?)

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L113      0 SEA FILE=BIOSIS ABB=ON  PLU=ON  L111 AND (SKIN OR DERM?)
L114      2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L111 AND (L109 OR MELANIN OR
MELANIZ? OR MELANIS?)
L115      3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L111 AND (L110 OR PENICILLIUM)

L117      4 SEA FILE=BIOSIS ABB=ON  PLU=ON  (L112 OR L113 OR L114 OR L115)

L118      0 SEA FILE=BIOSIS ABB=ON  PLU=ON  L111 AND "MELANIN BIOSYNTHESIS
INHIBIT?"
L119      4 SEA FILE=BIOSIS ABB=ON  PLU=ON  L117 OR L118

```

=> d his L133

(FILE 'EMBASE' ENTERED AT 17:21:37 ON 28 MAR 2008)

```

L133      5 S L131 OR L132

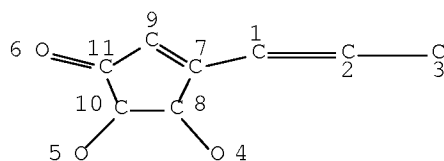
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=> d que L133

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L2      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  582-46-7/RN
L4      STR

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NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

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L6      9 SEA FILE=REGISTRY FAM FUL L4
L120    23 SEA FILE=EMBASE ABB=ON  PLU=ON  L2
L121    23 SEA FILE=EMBASE ABB=ON  PLU=ON  L6
L122    23 SEA FILE=EMBASE ABB=ON  PLU=ON  L120 OR L121
L123    4964 SEA FILE=EMBASE ABB=ON  PLU=ON  ("MELANI D"/CT OR MELANIDINE/CT
OR MELANIN/CT OR "MELANIZATION INHIBITING FACTOR"/CT OR
"MELANIZATION INHIBITING FACTOR: EC, ENDOGENOUS COMPOUND"/CT
OR "MELANIZATION INHIBITING PROTEIN"/CT OR "MELANIZATION
INHIBITING PROTEIN: EC, ENDOGENOUS COMPOUND"/CT OR "MELANIZATIO
N PROTEASE 1"/CT)
L124    6159 SEA FILE=EMBASE ABB=ON  PLU=ON  COSMETIC/CT
L125    2 SEA FILE=EMBASE ABB=ON  PLU=ON  L122 AND L123
L126    5 SEA FILE=EMBASE ABB=ON  PLU=ON  L122 AND MELANIN
L127    0 SEA FILE=EMBASE ABB=ON  PLU=ON  L122 AND L124
L128    0 SEA FILE=EMBASE ABB=ON  PLU=ON  L122 AND "MELANIN BIOSYNTHESIS
INHIBIT?"
L129    31 SEA FILE=EMBASE ABB=ON  PLU=ON  TERREIN
L130    31 SEA FILE=EMBASE ABB=ON  PLU=ON  L122 OR L129
L131    5 SEA FILE=EMBASE ABB=ON  PLU=ON  L130 AND (MELANIN? OR MELANIZ?
OR MELANIS?)
L132    5 SEA FILE=EMBASE ABB=ON  PLU=ON  (L125 OR L126 OR L127 OR L128)

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L133 5 SEA FILE=EMBASE ABB=ON PLU=ON L131 OR L132

=> dup rem L67 L92 L104 L119 L133

FILE 'HCAPLUS' ENTERED AT 17:31:04 ON 28 MAR 2008

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE 'BIOSIS' ENTERED AT 17:31:04 ON 28 MAR 2008

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FILE 'EMBASE' ENTERED AT 17:31:04 ON 28 MAR 2008

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FILE 'MEDLINE' ENTERED AT 17:31:04 ON 28 MAR 2008

PROCESSING COMPLETED FOR L67

PROCESSING COMPLETED FOR L92

PROCESSING COMPLETED FOR L104

PROCESSING COMPLETED FOR L119

PROCESSING COMPLETED FOR L133

L135 17 DUP REM L67 L92 L104 L119 L133 (12 DUPLICATES REMOVED)

ANSWERS '1-9' FROM FILE HCAPLUS

ANSWERS '10-14' FROM FILE BIOSIS

ANSWERS '15-17' FROM FILE EMBASE

Structure & text search results

=> d L135 1-9 ibib ed abs hitind hitstr

L135 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1974:504805 HCAPLUS Full-text

DOCUMENT NUMBER: 81:104805

ORIGINAL REFERENCE NO.: 81:16567a,16570a

TITLE: Synthesis of terrein, a metabolite of *Aspergillus terreus*

AUTHOR(S): Auerbach, Joseph; Weinreb, Steven M.

CORPORATE SOURCE: Dep. Chem., Fordham Univ., Bronx, NY, USA

SOURCE: Journal of the Chemical Society, Chemical Communications (1974), (8), 298-9
CODEN: JCCCAT; ISSN: 0022-4936

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 12 May 1984

GI For diagram(s), see printed CA Issue.

AB (+)-Terrein (I), a metabolite of *A. terreus*, was prepared in 9 steps from the epoxide II.

CC 24-4 (Alicyclic Compounds)

Section cross-reference(s): 10

IT 54192-03-9P

RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of)

IT 54192-03-9P

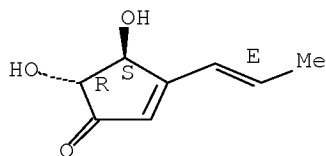
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of)

RN 54192-03-9 HCAPLUS

CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1E)-1-propenyl-, (4R,5S)-rel- (9CI)
(CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.



L135 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:540480 HCAPLUS Full-text

DOCUMENT NUMBER: 143:83184

TITLE: Terrein compound having melanin biosynthesis inhibitors and its preparation

INVENTOR(S): Yoo, Ick-Dong; Kim, Won-Gon; Ryoo, In-Ja; Kim, Jong-Pyung; Lee, Sangku; Park, Seo-Hyoung; Kim, Dong-Seok; Park, Kyoung-Chan

PATENT ASSIGNEE(S): Korea Research Institute of Bioscience and Biotechnology, S. Korea; Welskin Co., Ltd.

SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005055995	A1	20050623	WO 2004-KR2677	20041019 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1691796	A1	20060823	EP 2004-793535	20041019 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1925848	A	20070307	CN 2004-80036912	20041019 <--
JP 2007513941	T	20070531	JP 2006-543731	20041019 <--
US 2007128136	A1	20070607	US 2006-596211	20060602 <--
PRIORITY APPLN. INFO.:			KR 2003-90611	A 20031212 <--
			WO 2004-KR2677	W 20041019

ED Entered STN: 23 Jun 2005

AB The present invention relates to a melanin biosynthesis inhibitor containing terrein compound as an effective ingredient. The terrein compound can be easily separated from *Penicillium* sp. KCTC 26245, a fungal strain inhabiting domestic soil. It does not directly inhibit tyrosinase but inhibits the expression of MITF (microphthalmia-associated transcription factor) by activating ERK (extracellular signal-regulated kinase) in melanin chromatocytes to give whitening effect. So, the melanin biosynthesis inhibiting effect of the compound is much greater than that of any other conventional inhibitors, and further the effect can be raised when the compound is used together with other inhibitors, owing to their different mechanisms. Thus, the compound of the present invention can be effectively used as a skin trouble treating agent, a skin whitening agent and a browning inhibitor.

IC ICM A61K031-122

CC 62-4 (Essential Oils and Cosmetics)

Section cross-reference(s): 16

ST terrein *Penicillium* cosmetic melanin inhibitor

IT Transcription factors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (MITF (microphthalmia-associated transcription factor); terrein
 compound having melanin biosynthesis
 inhibitors and its preparation)

IT Cosmetics

(skin-lightening; terrein compound having
 melanin biosynthesis inhibitors and its
 preparation)

IT Melanocyte

(terrein compound having melanin biosynthesis
 inhibitors and its preparation)

IT Melanins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (terrein compound having melanin biosynthesis

inhibitors and its preparation)

IT Penicillium
(terrein compound having melanin biosynthesis inhibitors and its preparation from Penicillium)

IT 582-46-7P, Terrein
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); COS (Cosmetic use); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); USES (Uses)
(terrein compound having melanin biosynthesis inhibitors and its preparation)

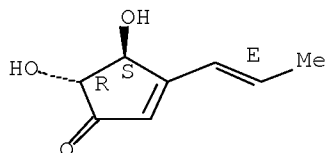
IT 142243-02-5, Extracellular signal-regulated kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(terrein compound having melanin biosynthesis inhibitors and its preparation)

IT 582-46-7P, Terrein
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); COS (Cosmetic use); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); USES (Uses)
(terrein compound having melanin biosynthesis inhibitors and its preparation)

RN 582-46-7 HCAPLUS

CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1E)-1-propen-1-yl-, (4S,5R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 142243-02-5, Extracellular signal-regulated kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(terrein compound having melanin biosynthesis inhibitors and its preparation)

RN 142243-02-5 HCAPLUS

CN Kinase (phosphorylating), mitogen-activated protein (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L135 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:623846 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 137:337687

TITLE: Phosphonate-mediated synthesis of biologically active cyclopentanones and cyclopentenones

AUTHOR(S): Mikolajczyk, Marian

CORPORATE SOURCE: Center of Molecular and Macromolecular Studies, Polish Academy of Sciences, Lodz, 90-363, Pol.

SOURCE: Phosphorus, Sulfur and Silicon and the Related Elements (2002), 177(6-7), 1839-1842
CODEN: PSSLEC; ISSN: 1042-6507

PUBLISHER: Taylor & Francis Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

ED Entered STN: 19 Aug 2002

AB A review. The synthesis and reactivity of 3-(phosphorylmethyl)cyclopent-2-enones as well as a complete desymmetrization of meso-tartaric acid are discussed as a platform for developing the synthesis of racemic rosaprostol and enantiomeric forms of prostaglandin B1 Me ester, isoterrein, and neplanocin A.

CC 26-0 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 33

IT 28186-87-0P, (+)-Prostaglandin B1 methyl ester 72877-50-0P, Neplanocin A
180682-72-8P, (-)-Isoterrein 180682-73-9P,
(+)-Isoterrein 218917-12-5P, (+)-Rosaprostol 294888-38-3P,
(-)-Prostaglandin B1 methyl ester

RL: SPN (Synthetic preparation); PREP (Preparation)
(phosphonate-mediated synthesis of biol. active cyclopentanones and cyclopentenones)

IT 180682-72-8P, (-)-Isoterrein 180682-73-9P,
(+)-Isoterrein

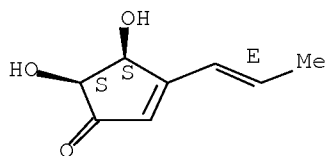
RL: SPN (Synthetic preparation); PREP (Preparation)
(phosphonate-mediated synthesis of biol. active cyclopentanones and cyclopentenones)

RN 180682-72-8 HCAPLUS

CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1E)-1-propenyl-, (4S,5S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.

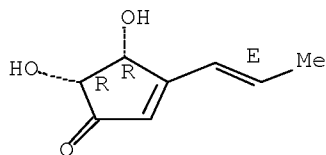


RN 180682-73-9 HCAPLUS

CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1E)-1-propenyl-, (4R,5R)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L135 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:473439 HCAPLUS Full-text
DOCUMENT NUMBER: 125:195253

10/596,211

TITLE: The first synthesis of enantiopure (-)- and (+)-isoterrein from optically inactive meso-tartaric acid

AUTHOR(S): Mikolajczyk, Marian; Mikina, Maciej; Wieczorek, Michal W.; Blaszczyk, Jaroslaw

CORPORATE SOURCE: Centre Molecular Macromolecular Studies, Polish Academy of Sciences, Lodz, 90-363, Pol.

SOURCE: Angewandte Chemie, International Edition in English (1996), 35(13/14), 1560-1562
CODEN: ACIEAY; ISSN: 0570-0833

PUBLISHER: VCH

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 10 Aug 1996

AB Both (-)- and (+)-isoterrein were prepared from meso-tartaric acid by asymmetrization by ketalization with camphor.

CC 26-6 (Biomolecules and Their Synthetic Analogs)

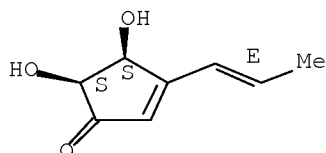
IT 180682-72-8P, (-)-Isoterrein 180682-73-9P, (+)-Isoterrein
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of enantiopure (-)- and (+)-isoterrein from meso-tartaric acid)

IT 180682-72-8P, (-)-Isoterrein 180682-73-9P, (+)-Isoterrein
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of enantiopure (-)- and (+)-isoterrein from meso-tartaric acid)

RN 180682-72-8 HCAPLUS

CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1E)-1-propenyl-, (4S,5S)- (9CI) (CA INDEX NAME)

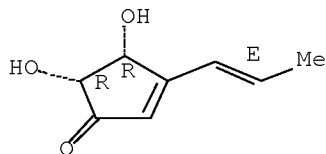
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 180682-73-9 HCAPLUS

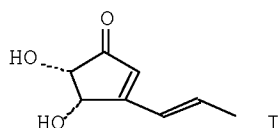
CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1E)-1-propenyl-, (4R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



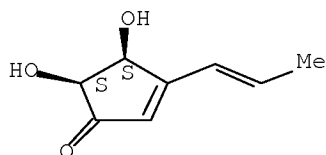
10/596,211

ACCESSION NUMBER: 1994:216735 HCAPLUS Full-text
 DOCUMENT NUMBER: 120:216735
 TITLE: A general approach to the synthesis of functionalized cycloalkenones. Total synthesis of iso-terrein
 AUTHOR(S): Mikina, Maciej; Mikolajczyk, Marian
 CORPORATE SOURCE: Cent. Mol. Macromol. Stud., Pol. Acad. Sci., Lodz, 90-363, Pol.
 SOURCE: Phosphorus, Sulfur and Silicon and the Related Elements (1993), 75(1-4), 39-42
 CODEN: PSSLEC; ISSN: 1042-6507
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 30 Apr 1994
 GI



AB A symposium lecture with 9 refs. The synthesis and chemical behavior of bis- β -ketophosphonates $(RO)_2P(O)CH_2CO(CH_2)_nCH_2COCH_2P(O)(OR)_2$ ($R = Me, Et; n = 1-3$) are described. A new approach to the synthesis of chiral iso-terrein (I) was developed which utilizes bis- β -ketophosphonate chemical
 CC 24-1 (Alicyclic Compounds)
 Section cross-reference(s): 26, 29
 IT 84196-90-7P 108264-48-8P 153983-75-6P 154096-62-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 IT 154096-62-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)
 RN 154096-62-5 HCAPLUS
 CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1-propenyl)-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.
 Double bond geometry unknown.

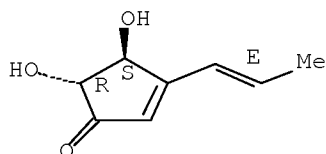


L135 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1990:115080 HCAPLUS Full-text
 DOCUMENT NUMBER: 112:115080
 TITLE: Gradient high-performance liquid chromatography using alkylphenone retention indices of insecticidal

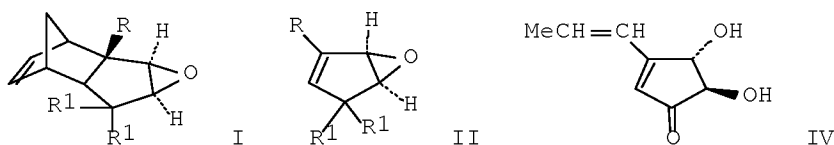
10/596,211

extracts of *Penicillium* strains
AUTHOR(S): Russell, R.; Paterson, M.; Kemmelmeier, Carlos
CORPORATE SOURCE: Int. Mycol. Inst., CAB, Kew/Surrey, TW9 3AF, UK
SOURCE: Journal of Chromatography (1989), 483,
153-68
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 31 Mar 1990
AB Purified exts. of 4 *Penicillium* strains which were active against the insect pest *Spodoptera littoralis* were analyzed by gradient HPLC for secondary metabolites using alkylphenone retention indexes. HPLC of pure secondary metabolite stds. detected previously in the exts. by TLC was undertaken in order to obtain bracketed retention indexes. More metabolites were detected by HPLC than by TLC, although some compds. detected by TLC in some strains were not detected by this HPLC method. A minority of metabolites were exclusive to each strain, and most were produced by >1 strain. The profiles were more characteristic of each strain when only the larger peaks were considered. This emphasizes the importance of detection limits in secondary metabolite anal. Some of the implications of these analyses to fungus toxicity and systematic mycol. are discussed.
CC 9-3 (Biochemical Methods)
Section cross-reference(s): 5, 10
IT 81-84-5, 1H,3H-Naphtho[1,8-cd]pyran-1,3-dione 90-65-3, Penicillic acid
126-07-8, Griseofulvin 129-24-8, Viridicatin 149-29-1, Patulin
303-47-9, Ochratoxin A 476-56-2, Islandicin 476-57-3, Erythroglaucin
480-64-8 481-74-3 495-08-9 501-30-4, Kojic acid 518-75-2, Citrinin
567-61-3, 6-Methylsalicylic acid 570-03-6, Terrestric acid
582-46-7, Terrein 602-06-2, Skyrin 1685-91-2,
Xanthomegnin 3733-72-0, Griseophenone C 11042-38-9, Xanthocillin
12627-35-9, Penitrem A 15222-53-4, Lichexanthone 15265-28-8,
Palitantin 18172-33-3, Cyclopiazonic acid 20007-85-6, Cyclophenol
20007-87-8, Cyclophenin 20716-98-7, Norlichexanthone 21794-01-4,
Rubratoxin B 22775-52-6, Mycelianamide 23402-09-7, Brevianamide A
24280-93-1, Mycophenolic acid 25186-77-0, Pachybasic acid 29119-03-7,
Frequentin 31077-93-7, Purpurogenone 33404-61-4, Carlosic acid
38747-39-6 39277-41-3, Viridicatum toxin 55625-78-0, Viomellein
56299-00-4, PR-toxin 58735-64-1, Roquefortine C 58735-66-3,
Roquefortine D 58800-19-4, Roquefortine A 58800-20-7, Roquefortine B
69448-97-1, Lapidosin 70553-75-2, Aflatrem 79297-77-1,
Desacetylpebrolide 106061-05-6 106061-06-7
RL: PROC (Process)
(separation of, of *Penicillium* by HPLC)
IT 582-46-7, Terrein
RL: PROC (Process)
(separation of, of *Penicillium* by HPLC)
RN 582-46-7 HCAPLUS
CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1E)-1-propen-1-yl-, (4S,5R)- (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L135 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1982:142527 HCAPLUS Full-text
 DOCUMENT NUMBER: 96:142527
 ORIGINAL REFERENCE NO.: 96:23429a,23432a
 TITLE: An efficient stereospecific total synthesis of
 (\pm)-terrein
 AUTHOR(S): Klunder, A. J. H.; Bos, W.; Zwanenburg, B.
 CORPORATE SOURCE: Dep. Org. Chem., Univ. Nijmegen, Nijmegen, 6525 ED,
 Neth.
 SOURCE: Tetrahedron Letters (1981), 22(45), 4557-60
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 12 May 1984
 GI



AB Flash vacuum pyrolysis of the tricyclodecenone epoxide I ($R = \text{CH:CHMe}$, $R_{12} = \text{O}$) and of the acetals I ($R = \text{CHO}$, CH:CHMe ; $R_1 = \text{OMe}$) gave the cyclopentadienone epoxide II ($R = \text{CH:CHMe}$, $R_{12} = \text{O}$) (III) and the acetals II ($R = \text{CHO}$, CH:CHMe ; $R_1 = \text{OMe}$), resp. II were suitable precursors for the title compound IV. Thus, hydrolysis of III in Me_2CO containing H_2SO_4 for 4 days at room temperature gave 55% IV.

CC 26-6 (Biomolecules and Their Synthetic Analogs)
 Section cross-reference(s): 22, 24

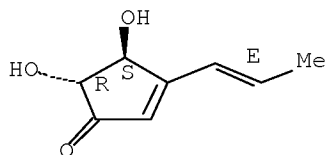
IT 54192-03-9P
 RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
 (stereospecific total synthesis of)

IT 54192-03-9P
 RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
 (stereospecific total synthesis of)

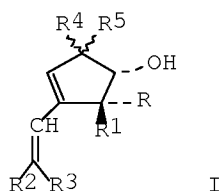
RN 54192-03-9 HCAPLUS

CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1E)-1-propenyl-, (4R,5S)-rel- (9CI)
 (CA INDEX NAME)

Relative stereochemistry.
 Double bond geometry as shown.



L135 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1977:484577 HCAPLUS Full-text
 DOCUMENT NUMBER: 87:84577
 ORIGINAL REFERENCE NO.: 87:13435a,13438a
 TITLE: Photochemical transformations. Part 35. A simple
 synthesis of racemic terrein
 AUTHOR(S): Barton, Derek H. R.; Hulshof, Lumbertus A.
 CORPORATE SOURCE: Chem. Dep., Imp. Coll., London, UK
 SOURCE: Journal of the Chemical Society, Perkin Transactions
 1: Organic and Bio-Organic Chemistry (1972-1999) (1977), (9), 1103-6
 CODEN: JCPRB4; ISSN: 0300-922X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 ED Entered STN: 12 May 1984
 GI



AB Photochem. ring contraction in the presence of NaBH₃CN of 5-hydroxy-2-[(E)-propenyl]-4-pyrone, prepared from the 2-chloromethyl analog by sequential treatment with PPh₃ and MeCHO, gave 7.5% terrein (I; R = R₃ = H, R₁ = OH, R₂ = Me, R₄R₅ = O). The photolysis also gave 24.7% I (R = OH, R₁ = R₃ = H, R₂ = Me, R₄R₅ = O), 1.4% I (R = R₃ = H, R₁ = OH, R₂ = Me, R₄, R₅ = H, OH), and 3.4% I (R = R₂ = H, R₁ = OH, R₃ = Me, R₄R₅ = O).

CC 24-4 (Alicyclic Compounds)
 Section cross-reference(s): 27

IT 63861-22-3P 63861-23-4P 63903-20-8P 63903-21-9P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

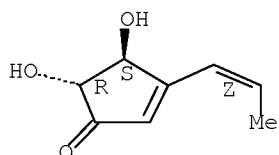
IT 54192-03-9P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, by photochem. ring contraction of pyrone derivative)

IT 63903-20-8P 63903-21-9P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 63903-20-8 HCAPLUS

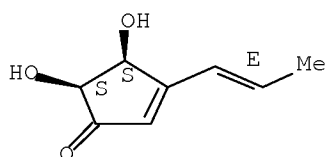
CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1-propenyl)-,
 [3(Z), 4 α , 5 β]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
 Double bond geometry as shown.



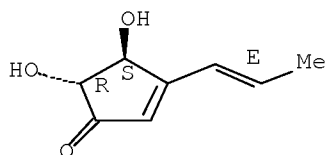
RN 63903-21-9 HCAPLUS
 CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1-propenyl)-,
 [3(E), 4 α , 5 α]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
 Double bond geometry as shown.



IT 54192-03-9F
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, by photochem. ring contraction of pyrone derivative)
 RN 54192-03-9 HCAPLUS
 CN 2-Cyclopenten-1-one, 4,5-dihydroxy-3-(1E)-1-propenyl-, (4R,5S)-rel- (9CI)
 (CA INDEX NAME)

Relative stereochemistry.
 Double bond geometry as shown.



L135 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1972:431343 HCAPLUS Full-text
 DOCUMENT NUMBER: 77:31343
 ORIGINAL REFERENCE NO.: 77:5215a,5218a
 TITLE: Humic acids from fungal origin. I. Infrared spectra
 AUTHOR(S): Saiz-Jimenez, C.; Martin Martinez, F.
 CORPORATE SOURCE: Cent. Edafol. Biol. Apl. Cuarto, Seville, Spain
 SOURCE: Anales de Edafologia y Agrobiologia (1972),
 31(1-2), 133-41
 CODEN: AEDAAB; ISSN: 0365-1797
 DOCUMENT TYPE: Journal
 LANGUAGE: Spanish
 ED Entered STN: 12 May 1984

AB A strain of *Penicillium* and a strain of *Alternaria chartarum* were isolated from black soil in Andalusia and incubated in Czapek-Dox solution or mineral solution supplemented with glucose and asparagine, at 25°, for 6 months. Filtrates were then acidified to pH 1 and ppts. prepared for examination at 4000 to 900 cm⁻¹. Humic acids isolated from the soil showed strong bands between 1400 and 1700 cm⁻¹, revealing prevalence of carboxylic groups (absorbing mainly around 1709 cm⁻¹). Humic acids from fungi absorbed weakly about 1709 cm⁻¹. The *Penicillium* species first synthesized red-pigments, which progressively darkened into lignin-like polymers. *A. chartarum* synthesized melanin which was released into the medium following autolysis.

CC 10-1 (Microbial Biochemistry)

=> d L135 10-17 ibib ab hit

L135 ANSWER 10 OF 17 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 4

ACCESSION NUMBER: 2005:164080 BIOSIS Full-text
DOCUMENT NUMBER: PREV200500158655
TITLE: Synthesis and melanin biosynthesis
inhibitory activity of (+/-)-terrein
produced by *Penicillium* sp 20135.
AUTHOR(S): Lee, Sangku; Kim, Won-Gon; Kim, Eungsoo; Ryoo, In-Ja; Lee,
Hyeong Kyu; Kim, Jae Nyoung; Jung, Sang-Hun; Yoo, Ick-Dong
[Reprint Author]
CORPORATE SOURCE: Korea Res Inst Biosci and Biotechnol, 52 Oun,Yusong,
Taejon, 305333, South Korea
idyoo@kribb.re.kr
SOURCE: Bioorganic & Medicinal Chemistry Letters, (January 17 2005)
Vol. 15, No. 2, pp. 471-473. print.
CODEN: BMCLE8. ISSN: 0960-894X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Apr 2005
Last Updated on STN: 27 Apr 2005
AB Terrein was isolated from *Penicillium* sp. 20135, prepared by a practical
synthetic way, and evaluated first time for its melanin biosynthesis
inhibitory activity. Copyright 2004 Elsevier Ltd. All rights reserved.
TI Synthesis and melanin biosynthesis inhibitory
activity of (+/-)-terrein produced by *Penicillium* sp 20135.
AB Terrein was isolated from *Penicillium* sp. 20135, prepared by a practical
synthetic way, and evaluated first time for its melanin biosynthesis
inhibitory activity. Copyright 2004 Elsevier Ltd. All rights reserved.
IT Major Concepts
Biochemistry and Molecular Biophysics; Integumentary System (Chemical
Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
epidermis: integumentary system; keratinocyte: integumentary system;
melanocyte: integumentary system
IT Chemicals & Biochemicals
melanin: biosynthesis; terren
ORGN Classifier
Fungi Imperfecti or Deuteromycetes 15500
Super Taxa
Fungi; Plantae
Organism Name
Penicillium (genus): strain-20135
Taxa Notes
Fungi, Microorganisms, Nonvascular Plants, Plants
RN 582-46-7 (terrein)

L135 ANSWER 11 OF 17 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN DUPLICATE 5

ACCESSION NUMBER: 2005:58304 BIOSIS Full-text
DOCUMENT NUMBER: PREV200500052127
TITLE: Terrein: a new melanogenesis inhibitor and its mechanism.
AUTHOR(S): Park, S.-H.; Kim, D.-S.; Kim, W.-G.; Ryoo, I.-J.; Lee, D.-H.; Huh, C.-H.; Youn, S.-W.; Yoo, I.-D.; Park, K.-C.
[Reprint Author]
CORPORATE SOURCE: Bundang HospDept Dermatol, Seoul Natl Univ, 300 Gumi Dong, Seongnam Si, Kyoungki Do, 463707, South Korea
gcpark@snu.ac.kr
SOURCE: CMLS Cellular and Molecular Life Sciences, (November 2004)
Vol. 61, No. 22, pp. 2878-2885. print.
ISSN: 1420-682X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Feb 2005
Last Updated on STN: 3 Feb 2005

AB Terrein is a bioactive fungal metabolite whose effects are almost unknown. In this study, we found for the first time that terrein has a strong hypopigmentary effect in a spontaneously immortalized mouse melanocyte cell line, Mel-Ab. Treatment of Mel-Ab cells with terrein (10 - 100 μ M) for 4 days significantly reduced melanin levels in a dose-dependent manner. In addition, terrein at the same concentration also reduced tyrosinase activity. We then investigated whether terrein influences the extracellular signal-regulated protein kinase (ERK) pathway and the expression of microphthalmia-associated transcription factor (MITF), which is required for tyrosinase expression. Terrein was found to induce sustained ERK activation and MITF down-regulation, and luciferase assays showed that terrein inhibits MITF promoter activity in a dose-dependent manner. To elucidate the correlation between ERK pathway activation and a decreased MITF transcriptional level, PD98059, a specific inhibitor of the ERK pathway, was applied before terrein treatment and found to abrogate the terrein-induced MITF attenuation. Terrein also reduced the tyrosinase protein level for at least 72 h. These results suggest that terrein reduces melanin synthesis by reducing tyrosinase production via ERK activation, and that this is followed by MITF down-regulation.

TI Terrein: a new melanogenesis inhibitor and its mechanism.

AB Terrein is a bioactive fungal metabolite whose effects are almost unknown. In this study, we found for the first time that terrein has a strong hypopigmentary effect in a spontaneously immortalized mouse melanocyte cell line, Mel-Ab. Treatment of Mel-Ab cells with terrein (10 - 100 μ M) for 4 days significantly reduced melanin levels in a dose-dependent manner. In addition, terrein at the same concentration also reduced tyrosinase activity. We then investigated whether terrein influences the extracellular signal-regulated protein kinase (ERK) pathway and the expression of microphthalmia-associated transcription factor (MITF), which is required for tyrosinase expression. Terrein was found to induce sustained ERK activation and MITF down-regulation, and luciferase assays showed that terrein inhibits MITF promoter activity in a dose-dependent manner. To elucidate the correlation between ERK pathway activation and a decreased MITF transcriptional level, PD98059, a specific inhibitor of the ERK pathway, was applied before terrein treatment and found to abrogate the terrein-induced MITF attenuation. Terrein also reduced the tyrosinase protein level for at least 72 h. These results suggest that terrein reduces melanin synthesis by reducing tyrosinase production via ERK activation, and that this is followed by MITF down-regulation.

IT Major Concepts

Biochemistry and Molecular Biophysics; Integumentary System (Chemical Coordination and Homeostasis)

IT Chemicals & Biochemicals

MITF promoter; PD98059: enzyme inhibitor-drug; extracellular signal-regulated protein kinase [EC 2.7.1.37]; melanin; microphthalmia-associated transcription factor [MITF]; terrein : fungal metabolite; tyrosinase

RN 167869-21-8 (PD98059)

142243-02-5 (extracellular signal-regulated protein kinase)

9026-43-1 (extracellular signal-regulated protein kinase)

142243-02-5 (EC 2.7.1.37)

9026-43-1 (EC 2.7.1.37)

582-46-7 (terrein)

9002-10-2 (tyrosinase)

L135 ANSWER 12 OF 17 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 1991:53776 BIOSIS Full-text

DOCUMENT NUMBER: PREV199191032057; BA91:32057

TITLE: A TOTAL SYNTHESIS OF RACEMIC AND OPTICALLY ACTIVE TERREIN TRANS-4 5 DIHYDROXY-3E-1-PROPENYL-2-CYCLOPENTEN-1-ONE.

AUTHOR(S): KOLB H C [Reprint author]; HOFFMANN H M R

CORPORATE SOURCE: DEP CHEM, IMPERIAL COLLEGE SCI TECHNOL MED, LONDON SW7 2AY, ENGLAND, UK

SOURCE: Tetrahedron Asymmetry, (1990) Vol. 1, No. 4, pp. 237-250. CODEN: TASYE3. ISSN: 0957-4166.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: ENGLISH

ENTRY DATE: Entered STN: 10 Jan 1991

Last Updated on STN: 10 Jan 1991

AB Two routes to terrein (1), employing a novel ring contraction of 6-alkoxy-2,3-dihydro-6H-pyran-3-ones (5, 13) are described. Separation into enantiomers was carried out by classical resolution via diastereomeric camphanic acid ester intermediates (14, 15). A new method for cleavage of the 2-(trimethylsilyl) ethyl protecting group in the presence of acid and base sensitive functionality is reported.

IT Miscellaneous Descriptors

ASPERGILLUS PENICILLIUM ANTIBACTERIAL AGENT AGRICULTURAL APPLICATIONS

RN 582-46-7 (TERREIN)

L135 ANSWER 13 OF 17 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 1979:119563 BIOSIS Full-text

DOCUMENT NUMBER: PREV197917059563; BR17:59563

TITLE: TERREIN AN OPTICALLY ACTIVE PROSTAGLANDIN SYNTHON OF FUNGAL ORIGIN PART 2 CHEMICAL CONVERSION TO 4 R ACETOXY-2 CYCLO PENTENONE.

AUTHOR(S): MITSCHER L A; CLARK G W III; HUDSON P B

SOURCE: Tetrahedron Letters, (1978) No. 29, pp. 2553-2556. CODEN: TELEAY. ISSN: 0040-4039.

DOCUMENT TYPE: Article

FILE SEGMENT: BR

LANGUAGE: Unavailable

TI TERREIN AN OPTICALLY ACTIVE PROSTAGLANDIN SYNTHON OF FUNGAL ORIGIN PART 2 CHEMICAL CONVERSION TO 4 R ACETOXY-2 CYCLO PENTENONE.

RN 582-46-7 (TERREIN)

28982-58-3 (CYCLO PENTENONE)

L135 ANSWER 14 OF 17 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN

ACCESSION NUMBER: 1974:146707 BIOSIS Full-text
DOCUMENT NUMBER: PREV197457046407; BA57:46407
TITLE: SIMULTANEOUS DETECTION OF METABOLITES FROM SEVERAL
TOXIGENIC FUNGI.
AUTHOR(S): PERO R W; HARVAN D
SOURCE: Journal of Chromatography, (1973) Vol. 80, No. 2, pp.
255-258.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable
IT Miscellaneous Descriptors
ALTERNARIA-SP ASPERGILLUS-SP PENICILLIUM-SP HUMAN ANIMAL
FOODSTUFFS GAS CHROMATOGRAPHY FLAME IONIZATION DETECTOR ERYTHRITOL
MANNITOL PALMITIC-ACID STEARIC-ACID SUCCINIC-ACID KOJIC-ACID ALTENUENE
ALTERNARIOL PATULIN PENICILLIC-ACID TERREIN

RN 149-32-6 (ERYTHRITOL)
69-65-8Q (MANNITOL)
87-78-5Q (MANNITOL)
57-10-3 (PALMITIC-ACID)
57-11-4 (STEARIC-ACID)
110-15-6 (SUCCINIC-ACID)
501-30-4 (KOJIC-ACID)
29752-43-0 (ALTENUENE)
641-38-3 (ALTERNARIOL)
149-29-1 (PATULIN)
90-65-3Q (PENICILLIC-ACID)
17397-87-4Q (PENICILLIC-ACID)
582-46-7 (TERREIN)

L135 ANSWER 15 OF 17 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights
reserved on STN DUPLICATE 1

ACCESSION NUMBER: 2008089794 EMBASE Full-text
TITLE: The hypopigmentary action of KI-063 (a new tyrosinase
inhibitor) combined with terrein.
AUTHOR: Kim D.-S.; Lee S.; Lee H.-K.; Park S.-H.; Ryoo I.-J.; Yoo
I.-D.; Kwon S.-B.; Kwang J.B.; Na J.-I.; Park K.-C.
CORPORATE SOURCE: K.-C. Park, Department of Dermatology, Seoul National
University Bundang Hospital, 300 Gumi-Dong, Bundang-Gu,
Seongnam-Si, Kyongki-Do 463-707, Korea, Republic of.
gcpark@snu.ac.kr
SOURCE: Journal of Pharmacy and Pharmacology, (Mar 2008) Vol. 60,
No. 3, pp. 343-348.
Refs: 36
ISSN: 0022-3573 CODEN: JPPMAB
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 013 Dermatology and Venereology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Mar 2008
Last Updated on STN: 11 Mar 2008
AB Resorcinol derivatives are known to inhibit melanin synthesis. In this study,
resorcinol derivatives were synthesized and screened for their activity on
melanogenesis. KI-063 (a tyrosinase inhibitor) was examined for its effects
on melanogenesis using a spontaneously immortalized mouse melanocyte cell line
(Mel-Ab). In a cell-free system, KI-063 directly inhibited tyrosinase, the

rate-limiting melanogenic enzyme. Moreover, in a cell system, it inhibited melanin synthesis in a concentration-dependent manner. In addition, KI-063 inhibited the activity of cellular tyrosinase. Thus, this study examined the effects of a combination of KI-063 with terrein, an agent that down-regulates microphthalmia-associated transcription factor. The data suggest that KI-063 has an additive effect in combination with terrein. Thus, the suppression of tyrosinase activity by KI-063 and the inhibition of tyrosinase production by terrein appear to be an optimal combination for skin whitening. .COPYRGT. 2008 The Authors.

- TI The hypopigmentary action of KI-063 (a new tyrosinase inhibitor) combined with terrein.
- AB Resorcinol derivatives are known to inhibit melanin synthesis. In this study, resorcinol derivatives were synthesized and screened for their activity on melanogenesis. KI-063 (a tyrosinase inhibitor) was examined for its effects on melanogenesis using a spontaneously immortalized mouse melanocyte cell line (Mel-Ab). In a cell-free system, KI-063 directly inhibited tyrosinase, the rate-limiting melanogenic enzyme. Moreover, in a cell system, it inhibited melanin synthesis in a concentration-dependent manner. In addition, KI-063 inhibited the activity of cellular tyrosinase. Thus, this study examined the effects of a combination of KI-063 with terrein, an agent that down-regulates microphthalmia-associated transcription factor. The data suggest that KI-063 has an additive effect in combination with terrein. Thus, the suppression of tyrosinase activity by KI-063 and the inhibition of tyrosinase production by terrein appear to be an optimal combination for skin whitening. .COPYRGT. 2008 The Authors.
- CT Medical Descriptors:
 animal cell
 article
 cytotoxicity
 drug mechanism
 enzyme synthesis
 hypopigmentation
 melanogenesis
 mouse
 nonhuman
- CT Drug Descriptors:
 *enzyme inhibitor: PD, pharmacology
 *ki 063: CB, drug combination
 *ki 063: PD, pharmacology
 *monophenol monooxygenase
 *terrein: CB, drug combination
 *terrein: PD, pharmacology
- RN (monophenol monooxygenase) 9002-10-2; (terrein)
 131233-98-2, 54192-03-9, 582-46-7

L135 ANSWER 16 OF 17 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN DUPLICATE 2

ACCESSION NUMBER: 2007142058 EMBASE Full-text

TITLE: Approaches to identify inhibitors of melanin biosynthesis via the quality control of tyrosinase.

AUTHOR: Ando H.; Kondoh H.; Ichihashi M.; Hearing V.J.

CORPORATE SOURCE: Dr. V.J. Hearing, Laboratory of Cell Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, United States. hearingv@nih.gov

SOURCE: Journal of Investigative Dermatology, (Apr 2007) Vol. 127, No. 4, pp. 751-761.
 Refs: 146
 ISSN: 0022-202X E-ISSN: 1523-1747 CODEN: JIDEAE

PUBLISHER IDENT.: 5700683

COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 013 Dermatology and Venereology
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 13 Apr 2007
 Last Updated on STN: 13 Apr 2007

- AB Tyrosinase, a copper-containing glycoprotein, is the rate-limiting enzyme critical for melanin biosynthesis in specialized organelles termed melanosomes that are produced only by melanocytic cells. Inhibitors of tyrosinase activity have long been sought as therapeutic means to treat cutaneous hyperpigmentary disorders. Multiple potential approaches exist that could control pigmentation via the regulation of tyrosinase activity, for example: the transcription of its messenger RNA, its maturation via glycosylation, its trafficking to melanosomes, as well as modulation of its catalytic activity and/or stability. However, relatively little attention has been paid to regulating pigmentation via the stability of tyrosinase, which depends on its processing and maturation in the endoplasmic reticulum and Golgi, its delivery to melanosomes and its degradation via the ubiquitin-proteasome pathway and/or the endosomal/lysosomal system. Recently, it has been shown that carbohydrate modification, molecular chaperone engagement, and ubiquitylation all play pivotal roles in regulating the degradation/stability of tyrosinase. While such processes affect virtually all proteins, such effects on tyrosinase have immediate and dramatic consequences on pigmentation. In this review, we classify melanogenic inhibitory factors in terms of their modulation of tyrosinase function and we summarize current understanding of how the quality control of tyrosinase processing impacts its stability and melanogenic activity. .COPYRGHT. 2007 The Society for Investigative Dermatology.
- TI Approaches to identify inhibitors of melanin biosynthesis via the quality control of tyrosinase.
- CT Medical Descriptors:
 catalysis
 enzyme degradation
 genetic transcription
 human
 hyperpigmentation: DT, drug therapy
 *melanogenesis
 nonhuman
 oculocutaneous albinism: ET, etiology
 priority journal
 protein function
 protein processing
 quality control
 review
- CT Drug Descriptors:
 25 hydroxycholesterol: PD, pharmacology
 3beta (2 diethylaminoethoxy)androst 5 en 17 one
 agouti protein: PD, pharmacology
 arbutin: PD, pharmacology
 bisindolylmaleimide: PD, pharmacology
 bmy 28565
 broxuridine: PD, pharmacology
 ceramide: PD, pharmacology
 dihydrolipoate: PD, pharmacology
 dithiothreitol: PD, pharmacology
 ellagic acid: PD, pharmacology
 epigallocatechin gallate: PD, pharmacology
 ferritin: PD, pharmacology

glucosamine: PD, pharmacology
 glutathione: PD, pharmacology
 hydrogen peroxide: PD, pharmacology
 hydroquinone: DT, drug therapy
 hydroquinone: PD, pharmacology
 insulin: PD, pharmacology
 kojic acid: PD, pharmacology
 linoleic acid: DT, drug therapy
 linoleic acid: PD, pharmacology
 linoleic acid: TP, topical drug administration
 lysophosphatidic acid: PD, pharmacology
 miglustat: PD, pharmacology
 *monophenol monooxygenase: EC, endogenous compound
 phenylthiourea: PD, pharmacology
 sphingosine 1 phosphate: PD, pharmacology
 sphingosylphosphorylcholine: PD, pharmacology
 terrein: PD, pharmacology
 thiocetic acid: PD, pharmacology
 thujaplicin: PD, pharmacology
 transforming growth factor beta1: PD, pharmacology
 tumor necrosis factor alpha: PD, pharmacology
 unindexed drug

RN (25 hydroxycholesterol) 2140-46-7; (3beta (2 diethylaminoethoxy)androst 5
 en 17 one) 3039-71-2; (arbutin) 497-76-7; (broxuridine) 59-14-3;
 (dihydrolipoate) 462-20-4; (dithiothreitol) 3483-12-3; (ellagic acid)
 476-66-4; (epigallocatechin gallate) 989-51-5; (ferritin) 9007-73-2;
 (glucosamine) 3416-24-8, 4607-22-1; (glutathione) 70-18-8; (hydrogen
 peroxide) 7722-84-1; (hydroquinone) 123-31-9; (insulin) 9004-10-8; (kojic
 acid) 501-30-4; (linoleic acid) 1509-85-9, 2197-37-7, 60-33-3, 822-17-3;
 (miglustat) 72599-27-0; (monophenol monooxygenase) 9002-10-2;
 (phenylthiourea) 103-85-5; (sphingosine 1 phosphate) 26993-30-6;
 (sphingosylphosphorylcholine) 1670-26-4; (terreins)
 131233-98-2, 54192-03-9, 582-46-7; (thiocetic
 acid) 1077-29-8, 1200-22-2, 2319-84-8, 62-46-4; (thujaplicin) 499-44-5

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 reserved on STN DUPLICATE 3

ACCESSION NUMBER: 2005407791 EMBASE Full-text
 TITLE: Terrein, a melanin biosynthesis
 inhibitor, from *Penicillium* sp. 20135.
 AUTHOR: Kim W.-G.; Ryoo I.-J.; Park S.-H.; Kim D.-S.; Lee S.; Park
 K.-C.; Yoo I.-D.
 CORPORATE SOURCE: I.-D. Yoo, Korea Research Institute of Bioscience and
 Biotechnology, P.O. Box 115, Yusong, Daejeon 305-600,
 Korea, Republic of. idyoo@kribb.re.kr
 SOURCE: Journal of Microbiology and Biotechnology, (Aug 2005) Vol.
 15, No. 4, pp. 891-894.
 Refs: 21
 ISSN: 1017-7825 CODEN: JOMBES
 COUNTRY: Korea, Republic of
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 013 Dermatology and Venereology
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 004 Microbiology: Bacteriology, Mycology, Parasitology
 and Virology
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 22 Sep 2005
 Last Updated on STN: 22 Sep 2005

- AB In the course of screening a melanin biosynthesis inhibitor, terrein, 4,5-dihydroxy-3-propenyl-2-cyclopenten-1-one, was isolated from *Penicillium* sp. Terrein was found to have a strong inhibitory activity on melanin formation in B16 melanoma and melanocyte Mel-Ab cells. .COPYRGT. The Korean Society for Microbiology and Biotechnology.
- TI Terrein, a melanin biosynthesis inhibitor, from *Penicillium* sp. 20135.
- AB In the course of screening a melanin biosynthesis inhibitor, terrein, 4,5-dihydroxy-3-propenyl-2-cyclopenten-1-one, was isolated from *Penicillium* sp. Terrein was found to have a strong inhibitory activity on melanin formation in B16 melanoma and melanocyte Mel-Ab cells. .COPYRGT. The Korean Society for Microbiology and Biotechnology.
- CT Medical Descriptors:
 animal cell
 article
 cell line
 controlled study
 drug activity
 drug isolation
 drug mechanism
 drug potency
 drug screening
 drug structure
 melanocyte
 *melanogenesis
 melanoma
 mouse
 nonhuman
 **Penicillium*
 species
- CT Drug Descriptors:
 kojic acid: CM, drug comparison
 kojic acid: PD, pharmacology
 melanin: EC, endogenous compound
 phenylthiourea: CM, drug comparison
 phenylthiourea: PD, pharmacology
 *terrein: AN, drug analysis
 *terrein: CM, drug comparison
 *terrein: DV, drug development
 *terrein: TO, drug toxicity
 *terrein: EC, endogenous compound
 *terrein: PD, pharmacology
- RN (kojic acid) 501-30-4; (melanin) 8049-97-6; (phenylthiourea) 103-85-5; (terrein) 131233-98-2, 54192-03-9, 582-46-7

Full search history

=> d his full

(FILE 'HOME' ENTERED AT 16:09:27 ON 28 MAR 2008)

FILE 'HCAPLUS' ENTERED AT 16:09:44 ON 28 MAR 2008

L1 1 SEA ABB=ON PLU=ON US 20070128136/PN
 D L1
 D SCAN

FILE 'REGISTRY' ENTERED AT 16:10:36 ON 28 MAR 2008

L2 1 SEA ABB=ON PLU=ON 582-46-7/RN
 L3 0 SEA ABB=ON PLU=ON 582-46-7/CRN

FILE 'REGISTRY' ENTERED AT 16:11:33 ON 28 MAR 2008

L4 STR 582-46-7
 L5 0 SEA FAM SAM L4
 L6 9 SEA FAM FUL L4
 L7 1 SEA ABB=ON PLU=ON 142243-02-5/RN
 L8 0 SEA ABB=ON PLU=ON 142243-02-5/CRN

FILE 'HCAPLUS' ENTERED AT 16:12:43 ON 28 MAR 2008

L9 62 SEA ABB=ON PLU=ON L2
 L10 69 SEA ABB=ON PLU=ON L6
 L11 14053 SEA ABB=ON PLU=ON L7
 L12 QUE ABB=ON PLU=ON ((CYCLO(W)PENTADIEN? OR CYCLO(W)PENTAN? OR
 CYCLO(W)PENTEN?))
 L13 QUE ABB=ON PLU=ON ((SKIN? OR DERM? OR EPIDERM? OR COMPLEXTION
 ? OR COMPLEXION? OR CUTICL?)(3A)(TROUBLE OR CONDITION OR
 BLOTCH? OR SPOT? OR LIVER? OR AGING? OR AGE OR WHITEN? OR
 BROWN? OR MELANIN))
 L14 QUE ABB=ON PLU=ON ((BROWN? OR MELANIN)(3A)(SYNTHESE? OR
 INHIBIT?))
 L15 QUE ABB=ON PLU=ON PENICILLIUM(5A)(STRAIN OR "KCTC" OR
 "KCTC(W)262245")
 L16 QUE ABB=ON PLU=ON TERREIN
 L17 75 SEA ABB=ON PLU=ON TERREIN
 L18 1 SEA ABB=ON PLU=ON L9 AND L11
 L19 1 SEA ABB=ON PLU=ON L10 AND L11
 L20 0 SEA ABB=ON PLU=ON L9 AND L12
 L21 1 SEA ABB=ON PLU=ON L9 AND L13
 L22 4 SEA ABB=ON PLU=ON L9 AND L14
 L23 3 SEA ABB=ON PLU=ON L9 AND L15
 L24 7 SEA ABB=ON PLU=ON L10 NOT L9
 L25 0 SEA ABB=ON PLU=ON L24 AND L12
 L26 0 SEA ABB=ON PLU=ON L24 AND L13
 L27 1 SEA ABB=ON PLU=ON L24 AND L14
 L28 0 SEA ABB=ON PLU=ON L24 AND L15
 E TERREINS/CT
 L29 QUE ABB=ON PLU=ON ((LIVER? OR AGE OR AGING OR BROWN? OR
 OLD?)(3A)(SPOT? OR BLOTCH? OR MARK? OR SIGN? OR SKIN? OR
 HAND?))
 L30 0 SEA ABB=ON PLU=ON L9 AND L29
 L31 0 SEA ABB=ON PLU=ON L10 AND L29
 L32 0 SEA ABB=ON PLU=ON L17 AND L12
 L33 2 SEA ABB=ON PLU=ON L17 AND L13
 L34 6 SEA ABB=ON PLU=ON L17 AND L14
 L35 3 SEA ABB=ON PLU=ON L17 AND L15

L36 1712 SEA ABB=ON PLU=ON PENICILLIUM(5A) (STRAIN OR "KCTC" OR
 "KCTC (W) 262245")
 L37 3 SEA ABB=ON PLU=ON L36 AND L9
 L38 3 SEA ABB=ON PLU=ON L36 AND L10
 L39 3 SEA ABB=ON PLU=ON L36 AND L17
 L40 0 SEA ABB=ON PLU=ON L36 AND L12
 L41 1 SEA ABB=ON PLU=ON L36 AND L13
 L42 3 SEA ABB=ON PLU=ON L36 AND L14
 L43 12 SEA ABB=ON PLU=ON (L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR
 L24 OR L25 OR L26 OR L27 OR L28)
 L44 7 SEA ABB=ON PLU=ON (L30 OR L31 OR L32 OR L33 OR L34 OR L35)
 L45 4 SEA ABB=ON PLU=ON (L37 OR L38 OR L39 OR L40 OR L41 OR L42)
 L46 14 SEA ABB=ON PLU=ON (L43 OR L44 OR L45)
 L47 QUE ABB=ON PLU=ON AY<2004 OR PY<2004 OR PRY<2004 OR MY<2004
 OR REVIEW/DT
 L48 9 SEA ABB=ON PLU=ON L46 AND L47
 L49 69 SEA ABB=ON PLU=ON L9 OR L10
 L50 58 SEA ABB=ON PLU=ON L49 AND L47
 L51 56 SEA ABB=ON PLU=ON L50 AND TERREIN
 L52 0 SEA ABB=ON PLU=ON L51 AND "MELANIN BIOSYNTHESIS INHIBIT?"
 L53 1 SEA ABB=ON PLU=ON L51 AND "MELANIN BIOSYNTHESIS"
 L54 0 SEA ABB=ON PLU=ON L51 AND "MELANIN(3N) INHIBIT?"
 L55 1 SEA ABB=ON PLU=ON L51 AND MELANIN
 L56 9 SEA ABB=ON PLU=ON L51 AND BIOSYNTHESIS?
 L57 7 SEA ABB=ON PLU=ON L51 AND INHIBIT?
 L58 15 SEA ABB=ON PLU=ON (L52 OR L53 OR L54 OR L55 OR L56 OR L57)
 D L58 1-15 TI
 L59 1 SEA ABB=ON PLU=ON L58 AND (MELANIN OR SKIN OR DERM?)
 L60 0 SEA ABB=ON PLU=ON L51 AND L12
 L61 1 SEA ABB=ON PLU=ON L51 AND L13
 L62 1 SEA ABB=ON PLU=ON L51 AND L14
 L63 2 SEA ABB=ON PLU=ON L51 AND L15
 L64 2 SEA ABB=ON PLU=ON (L59 OR L60 OR L61 OR L62 OR L63)
 L65 9 SEA ABB=ON PLU=ON L64 OR L48
 D L65 1-9 TI
 L66 1 SEA ABB=ON PLU=ON L51 AND BIOSYNTH? AND MELANIN AND (INHIBIT?
 OR BLOCK?)
 D L66 TI
 L67 9 SEA ABB=ON PLU=ON L65 OR L66
 SAVE TEMP L67 BLA211HCTX/A
 E YOO I?/AU
 L68 160 SEA ABB=ON PLU=ON ("YOO ICH DONG"/AU OR "YOO ICK D"/AU OR
 "YOO ICK DOG"/AU OR "YOO ICK DONG"/AU OR "YOO ICK JONG"/AU OR
 "YOO ICKDONG"/AU)
 E KIM W?/AU
 E KIM WON?/AU
 E KIM WON GON/AU
 L69 79 SEA ABB=ON PLU=ON "KIM WON GON"/AU
 E RYOO IN JA/AU
 L70 46 SEA ABB=ON PLU=ON "RYOO IN JA"/AU
 E KIM JONG PYUNG
 E KIM JONG PYUNG/AU
 L71 52 SEA ABB=ON PLU=ON ("KIM JONG PYONG"/AU OR "KIM JONG PYUNG"/AU
)
 E LEE SANGKU
 E LEE SANGKU/AU
 L72 48 SEA ABB=ON PLU=ON "LEE SANGKU"/AU
 E LEE SANG KU
 E LEE SANG KU/AU
 L73 30 SEA ABB=ON PLU=ON "LEE SANG KU"/AU

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E PARK SEO HYOUNG/AU
L74 27 SEA ABB=ON PLU=ON ("PARK SEO HYEONG"/AU OR "PARK SEO
HYOUNG"/AU)
E PARK SEOHYOUNG/AU
L75 4 SEA ABB=ON PLU=ON ("PARK SEOHYOUNG"/AU OR "PARK SEOHYUNG"/AU)

E KIM DONG SEOK/AU
L76 210 SEA ABB=ON PLU=ON ("KIM DONG SEOCK"/AU OR "KIM DONG SEOG"/AU
OR "KIM DONG SEOK"/AU)
E KIM DONGSEOK/AU
E PARK KYOUNG CHAN/AU
L77 55 SEA ABB=ON PLU=ON "PARK KYOUNG CHAN"/AU
E PARK KYOUNGCHAN/AU
E YOO ICKDONG/AU
L78 1 SEA ABB=ON PLU=ON "YOO ICKDONG"/AU
E KIM WONGON/AU
L79 0 SEA ABB=ON PLU=ON L69 AND L69 AND L70 AND L71 AND (L72 OR
L73) AND (L74 OR L75) AND L76 AND L77 AND L78
L80 508 SEA ABB=ON PLU=ON (L68 OR L69 OR L70 OR L71 OR L72 OR L73 OR
L74 OR L75 OR L76 OR L77 OR L78)
L81 7 SEA ABB=ON PLU=ON L80 AND TERREIN
L82 6 SEA ABB=ON PLU=ON L80 AND (L9 OR L10)
L83 7 SEA ABB=ON PLU=ON L81 OR L82
D L83 1-7 AU
D L83 1-7 TI
SAVE TEMP L83 BLA211HCIN/A

FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 17:03:12 ON 28 MAR 2008

L84 44 SEA ABB=ON PLU=ON L9
L85 45 SEA ABB=ON PLU=ON L10
L86 45 SEA ABB=ON PLU=ON L84 OR L85
L87 45 SEA ABB=ON PLU=ON L86 AND TERREIN
L88 2 SEA ABB=ON PLU=ON L87 AND L12
L89 1 SEA ABB=ON PLU=ON L87 AND L13
L90 7 SEA ABB=ON PLU=ON L87 AND L14
L91 1 SEA ABB=ON PLU=ON L87 AND L15
L92 9 SEA ABB=ON PLU=ON (L88 OR L89 OR L90 OR L91)
D L92 1-9 TI
D L92 1-9 AU
L93 9 SEA ABB=ON PLU=ON L81
SAVE TEMP L92 BLA211MLTX/A
SAVE TEMP L93 BLA211MLIN/A
L94 0 SEA ABB=ON PLU=ON L87 AND COSMET?

FILE 'MEDLINE' ENTERED AT 17:08:02 ON 28 MAR 2008

E SKIN CARE AGENTS/CT
L95 2944 SEA ABB=ON PLU=ON "SKIN CARE"/CT
E COSMETICS/CT
L96 3922 SEA ABB=ON PLU=ON COSMETICS/CT
E MELANIN
E MELANIN/CT
L97 7428 SEA ABB=ON PLU=ON (MELANINS/CT OR "MELANINS: AA, ANALOGS &
DERIVATIVES"/CT OR "MELANINS: AG, AGONISTS"/CT OR "MELANINS:
AI, ANTAGONISTS & INHIBITORS"/CT OR "MELANINS: BI, BIOSYNTHESIS
"/CT OR "MELANINS: CH, CHEMISTRY"/CT OR "MELANINS: ME,
METABOLISM"/CT OR "MELANINS: PD, PHARMACOLOGY"/CT)
E PENICILLIUM/CT
L98 5353 SEA ABB=ON PLU=ON PENICILLIUM/CT
L99 0 SEA ABB=ON PLU=ON (L9 OR L10)
L100 39 SEA ABB=ON PLU=ON TERREIN?

10/596,211

L101 0 SEA ABB=ON PLU=ON L100 AND L95
L102 0 SEA ABB=ON PLU=ON L100 AND L96
L103 2 SEA ABB=ON PLU=ON L100 AND L97
L104 2 SEA ABB=ON PLU=ON L100 AND L98
L105 2 SEA ABB=ON PLU=ON L99 OR (L101 OR L102 OR L103 OR L104)

FILE 'BIOSIS' ENTERED AT 17:13:14 ON 28 MAR 2008

L106 19 SEA ABB=ON PLU=ON L2
L107 20 SEA ABB=ON PLU=ON L6
E SKIN CARE/CT
E SKIN CARE+ALL/CT
E COSMETICS/CT
L108 5886 SEA ABB=ON PLU=ON COSMETICS/CT
E MELANIN/CT
L109 5151 SEA ABB=ON PLU=ON ("MELANIELLA "/CT OR "MELANIFEROUS
ZONA"/CT OR MELANIN/CT OR "MELANIN "/CT OR "MELANIN A"/CT OR
"MELANIN AFFINITY"/CT OR "MELANIN ALLERGY"/CT OR "MELANIN
ANALOGUE"/CT OR "MELANIN ASSOCIATED ANTIGEN"/CT OR "MELANIN
BINDING PROPERTIES"/CT OR "MELANIN BIOSYNTHESIS"/CT OR
"MELANIN BIOSYNTHESIS DEHYDRATASE INHIBITOR"/CT OR "MELANIN
BIOSYNTHESIS GENES"/CT OR "MELANIN BIOSYNTHESIS INHIBITOR"/CT
OR "MELANIN BIOSYNTHESIS INHIBITOR-CONTAINING COMPOSITION"/CT
OR "MELANIN BIOSYNTHETIC ENZYMES"/CT OR "MELANIN BIOSYNTHETIC
PATHWAY INTERMEDIATE"/CT OR "MELANIN BLEACH"/CT OR "MELANIN
BLEACHING"/CT OR "MELANIN CELLS"/CT OR "MELANIN COLORATION"/CT
OR "MELANIN COLUMNS"/CT OR "MELANIN COMPLEX"/CT OR "MELANIN
COMPLEXES"/CT OR "MELANIN CONCENTRATING HORMONE"/CT OR
"MELANIN CONCENTRATING HORMONE 1"/CT OR "MELANIN CONCENTRATING
HORMONE 1 RECEPTOR"/CT OR "MELANIN CONCENTRATING HORMONE 2
RECEPTOR"/CT OR "MELANIN CONCENTRATING HORMONE ANTAGONIST"/CT
OR "MELANIN CONCENTRATING HORMONE ANTAGONIST 1"/CT OR "MELANIN
CONCENTRATING HORMONE ANTAGONISTS"/CT OR "MELANIN CONCENTRATING
HORMONE MESSENGER RNA"/CT OR "MELANIN CONCENTRATING HORMONE
MRNA"/CT OR "MELANIN CONCENTRATING HORMONE NEURONAL POPULATION"
/CT OR "MELANIN CONCENTRATING HORMONE PRECURSOR MRNA"/CT OR
"MELANIN CONCENTRATING HORMONE R1 ANTAGONIST"/CT OR "MELANIN
CONCENTRATING HORMONE RECEPTOR"/CT OR "MELANIN CONCENTRATING
HORMONE RECEPTOR 1"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR 1 ANTAGONIST"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR 1 ANTAGONISTS"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR 2"/CT OR "MELANIN CONCENTRATING HORMONE RECEPTOR
AGONISTS"/CT OR "MELANIN CONCENTRATING HORMONE RECEPTOR
ANTAGONIST"/CT OR "MELANIN CONCENTRATING HORMONE RECEPTOR
CHIMERIC PROTEIN"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR FUSION PROTEIN"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR LIGANDS"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR MESSENGER RNA"/CT OR "MELANIN CONCENTRATING HORMONE
RECEPTOR MRNA"/CT OR "MELANIN CONCENTRATING HORMONE RECEPTOR
POL
E PENICILLIUM/CT
L110 3 SEA ABB=ON PLU=ON PENICILLIUM/CT
L111 20 SEA ABB=ON PLU=ON L106 OR L107
L112 0 SEA ABB=ON PLU=ON L111 AND (L108 OR COSMETIC?)
L113 0 SEA ABB=ON PLU=ON L111 AND (SKIN OR DERM?)
L114 2 SEA ABB=ON PLU=ON L111 AND (L109 OR MELANIN OR MELANIZ? OR
MELANIS?)
L115 3 SEA ABB=ON PLU=ON L111 AND (L110 OR PENICILLIUM)
L116 17 SEA ABB=ON PLU=ON L111 AND L47
D L116 1-11 TI
L117 4 SEA ABB=ON PLU=ON (L112 OR L113 OR L114 OR L115)

10/596,211

L118 0 SEA ABB=ON PLU=ON L111 AND "MELANIN BIOSYNTHESIS INHIBIT?"
L119 4 SEA ABB=ON PLU=ON L117 OR L118
D L119 1-4 TI

FILE 'EMBASE' ENTERED AT 17:21:37 ON 28 MAR 2008

L120 23 SEA ABB=ON PLU=ON L2
L121 23 SEA ABB=ON PLU=ON L6
L122 23 SEA ABB=ON PLU=ON L120 OR L121
E MELANIN/CT
L123 4964 SEA ABB=ON PLU=ON ("MELANI D"/CT OR MELANIDINE/CT OR
MELANIN/CT OR "MELANIZATION INHIBITING FACTOR"/CT OR "MELANIZA
TION INHIBITING FACTOR: EC, ENDOGENOUS COMPOUND"/CT OR "MELANIZA
TION INHIBITING PROTEIN"/CT OR "MELANIZATION INHIBITING
PROTEIN: EC, ENDOGENOUS COMPOUND"/CT OR "MELANIZATION PROTEASE
1"/CT)
E COSMETICS/CT
E COSMETIC/CT
L124 6159 SEA ABB=ON PLU=ON COSMETIC/CT
L125 2 SEA ABB=ON PLU=ON L122 AND L123
L126 5 SEA ABB=ON PLU=ON L122 AND MELANIN
L127 0 SEA ABB=ON PLU=ON L122 AND L124
L128 0 SEA ABB=ON PLU=ON L122 AND "MELANIN BIOSYNTHESIS INHIBIT?"
L129 31 SEA ABB=ON PLU=ON TERREIN
L130 31 SEA ABB=ON PLU=ON L122 OR L129
L131 5 SEA ABB=ON PLU=ON L130 AND (MELANIN? OR MELANIZ? OR MELANIS?)

L132 5 SEA ABB=ON PLU=ON (L125 OR L126 OR L127 OR L128)
L133 5 SEA ABB=ON PLU=ON L131 OR L132
D L133 1-5 TI
D QUE L83
D QUE L93

FILE 'HCAPLUS, MEDLINE, BIOSIS' ENTERED AT 17:29:23 ON 28 MAR 2008

L134 10 DUP REM L83 L93 (6 DUPLICATES REMOVED)
ANSWERS '1-7' FROM FILE HCAPLUS
ANSWERS '8-10' FROM FILE MEDLINE
D L134 1-10 IBIB AB
D QUE L67
D QUE L92
D QUE L104
D QUE L119
D QUE L133

FILE 'HCAPLUS, BIOSIS, EMBASE, MEDLINE' ENTERED AT 17:31:04 ON 28 MAR 2008

L135 17 DUP REM L67 L92 L104 L119 L133 (12 DUPLICATES REMOVED)
ANSWERS '1-9' FROM FILE HCAPLUS
ANSWERS '10-14' FROM FILE BIOSIS
ANSWERS '15-17' FROM FILE EMBASE
D L135 1-9 IBIB ED ABS HITIND HITSTR
D L135 10-17 IBIB AB HIT

FILE HOME

FILE HCAPLUS

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FILE LAST UPDATED: 27 Mar 2008 (20080327/ED)

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FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 27 MAR 2008 HIGHEST RN 1010733-70-6
DICTIONARY FILE UPDATES: 27 MAR 2008 HIGHEST RN 1010733-70-6

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<http://www.cas.org/support/stngen/stdoc/properties.html>

FILE MEDLINE

FILE LAST UPDATED: 27 Mar 2008 (20080327/UP). FILE COVERS 1949 TO DATE.

MEDLINE has been updated with the National Library of Medicine's revised 2008 MeSH terms. See HELP RLOAD for details.

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FILE BIOSIS

FILE COVERS 1926 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 26 March 2008 (20080326/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE EMBASE

FILE COVERS 1974 TO 28 Mar 2008 (20080328/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

10/596,211

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Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE codes.

For further assistance, please contact your local helpdesk.

FILE DRUGU

FILE LAST UPDATED: 28 MAR 2008 <20080328/UP>

>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<

>>> THESAURUS AVAILABLE IN /CT <<<